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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,658	03/01/2004	Cheryl D. Blume	SOM700/4-4CIP2CON2DIV	9575

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EXAMINER

CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/790,658

Applicant(s)

BLUME ET AL.

Examiner

Lakshmi S Channavajjala

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 26 and 34-62 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 26 and 34-62 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3-1-04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

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DETAILED ACTION

Claims 1-25 and 27-33 have been canceled by preliminary amendment. New claims 34-62 have been added. Claims 26 and 34-62 are pending.

Claim Rejections - 35 USC § 112

Claims 26 and 34, 38-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims recite a method of treating “a condition” produced by immune system dysfunction that is associated with reduced levels of gamma-interferon production, comprising administering R(-) desmethylselegiline (DMS), wherein the administration leads to an increased production of gamma-interferon in the mammal. Instant claims are broad as they encompass a number of “conditions” that are stimulated or caused by immune dysfunction or immune deficiency.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: nature of the invention, breadth of the claims, state of the art, guidance of the specification, predictability of the art, and the working examples. All the factors have been considered with regard to the claim, with the most relevant factors discussed below.

Nature of the Invention: All rejected claims are drawn to a method of treating “a condition” produced by immune system dysfunction that is associated with reduced levels of gamma-interferon production, comprising administering R(-) desmethylselegiline (DMS),

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wherein the administration leads to an increased production of gamma-interferon in the mammal. The nature of the invention is extremely complex in that it encompasses anticipating multiple complex diseases or disorders and subsequently administering the instant composition. The breadth of the claims exacerbates the complex nature of the claims. The claim encompasses treating complex disorders that may have potential causes other than those disclosed in the specification. The term immune dysfunction is not necessarily manifested by one condition i.e., pathogenesis, disease or disorder. For instance, AIDS (also described in the instant invention) is a complex of diseases and conditions, which are not necessarily treatable.

State of the Art: The state of the art does not recognize the administration of compositions to treat disorders such as substance abuse, neurological conditions associated with increased monoamine oxidase, reduced dopamine uptake etc. The state of the art also recognizes treating specific infections or diseases by administering gamma -interferon or other immunomodulating interleukins or chemokines. However, the functioning of immune system in response to an infection or a disease or disorder is modulated by not one immunomodulator molecule but is a complex interplay of several interleukins or chemokines. Further, a reduction in gamma-interferon does not necessarily result in immune system dysfunction. This is particularly evident from the cited references (Immunology, 1996 and Shi et al, J. Immunology 2004) in the case of AIDS, which applicants claims as a condition caused by immune dysfunction and is associated with reduced gamma-interferon. Thus, the described or claimed conditions may or may not be caused by gamma-interferon reduction leading to immune dysfunction.

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Guidance of the Specification: The guidance given by the specification on how to treat the disorders is absent. Instant specification describes the effect of age on T cell function in terms of the levels of IL-2 and IFN-gamma. Further, the specification also describes the effect of DMS in restoring the levels of IL-2 and gamma-interferon. However, instant specification provides no guidance with respect to the procedure of administering instant composition to mammals for treating any or all of the disorders claimed. Instant specification also fails to provide any guidance or rationale showing that the claimed method is effective in completely treating any or all disorders produced by immune dysfunction, associated with reduced levels of gamma-IFN or to extrapolate the data provided to all immune dysfunction conditions, that are known to-date or yet to be discovered.

Predictability of the Art & The Amount of Experimentation Necessary: The specification lacks guidance from the prior art with regard to treating the claimed conditions, such that a completely effective treatment is ensured. Further, the state of the art recognizes that gamma-IFN levels need not necessarily be reduced in all immune dysfunction conditions or disorders. Thus, the lack of guidance from the specification together with unpredictability of reduced IFN levels in all immune dysfunctions (see above references), leads to further unpredictability of the efficacy of DMS in treating conditions produced by immune system dysfunction (associated with gamma-IFN). Therefore, the practitioner would turn to trial and error experimentation in order to determine the "conditions" caused by immune system dysfunction (associated with gamma-IFN) in mammals that would respond to the claimed method of treatment (employing the claimed composition). Therefore, undue experimentation becomes the burden of the practitioner.

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Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26 and 34, 38-62 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,033,682; claims 1-57 of U.S. Patent No. 6,348,208; claims 1-33 of U.S. Patent No. 6,419,948; claims 1-30 of U.S. Patent No. 6,562,365; claims 1-36 of U.S. Patent No. 6,699,495 and claims 1-26 of U.S. Patent No. 6,528,082. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Instant claims are directed to a method of treating a condition in a mammal produced by immune system dysfunction that is associated with reduced levels of gamma-IFN production, comprising administering at least 0.015 mg R(-)DMS so as to increase the gamma-IFN production in the mammal. Instant dependent claims recite immune dysfunction conditions such as infectious diseases, cancer, AIDS, age dependent etc.

Each of the above mentioned patent claims are directed to compositions comprising R(-) DMS and method of treating conditions such as Multiple sclerosis (patent '495), neoplastic conditions (patent '082), improvement or restoration of immune system function, Alzheimer's

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disease, ADHD (patents '365 & '948), restoration of immune system dysfunction ('208 & '682).

Accordingly, instant method of treating a condition is anticipated in view of all of the patented claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26 and 34, 38-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over f
Borbe (J. neural. Transm. Suppl. 1990) in view of Barton et al (J. Neurooncol.) and Balsa et al
(Biochem. Pharmacol. 1987).

Borbe teaches desmethylselegiline (DMS) and selegiline as effective MAO-B inhibitors, which irreversibly blocks MAO-B. Borbe also teaches oral administration of DMS in rats. However, Borbe does not specifically state that DMS is used for treating "a condition produced by immune system dysfunction that is associated with gamma-interferon production", as claimed. Further, Borbe also fails to teach the claimed enantiomer or specific disease conditions.

Barton et al (Barton) analyzed neurological complications in patients suffering from Kaposi's sarcoma and observed that patients suffered neurological dysfunction that included neoplastic involvement of nervous system, autoimmune disorders or opportunistic infections (abstract). Barton does not suggest any treatment for the above conditions, however, establishes a

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relation ship between acquired immune deficiency syndrome, autoimmune disorders, nervous system dysfunction and opportunistic infections.

Balsa et al teaches monoamine oxidase activities in lymphocytes (L) and granulocytes (G), particularly against 5-hydroxytryptamine, benzylamine, beta-phenyl ethylamine etc., as substrates. Balsa et al conclude from their experiments with deprenyl that monoamine oxidase (MAO) activity present in both L and G is predominantly of MAO-B form. Thus, Balsa shows the activity of MAO-B in lymphocytes and granulocytes, the cell types that play a key role in immune system function and Barton teaches that immune deficiency is related to conditions such as cancer, neurological dysfunction, infection and AIDS. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use DMS of Borbe for reducing the MAO-B activity in lymphocytes and granulocytes, which in turn play an important role in the development of immune deficient disorders such as Kaposi's' sarcoma, AIDS or other opportunistic infections because Barton associates immune dysfunction with conditions such as AIDS, Kaposi's' sarcoma etc., and Balsa teaches that activity of MAO-B is predominant in G and L cells , which can be effectively inhibited by deprenyl. One of an ordinary skill in the art would have expected DMS, a monoamine oxidase inhibitor, to be effective in treating AIDS, tumors, cancers and other immune deficient conditions by inhibiting the action of MAO-B of immune cells i.e., lymphocytes and granulocytes. While the above references do not explicitly state a reduction in the levels of gamma-IFN, absent showing the evidence to the contrary, it is the position of the examiner that the claimed composition implicitly restores the levels of gamma-IFN. Furthermore, optimization of claimed dosage of DMS and choosing the appropriate


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routes of administration, with an expectation to obtain the desired therapeutic effect would have been within the scope of a skilled artisan.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala

Examiner

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October 18, 2004